

What Is Claimed Is:

1. A composition comprising a first oligomer and a second oligomer, wherein:
 - at least a portion of said first oligomer is capable of hybridizing with at least a portion of said second oligomer,
 - at least a portion of said first oligomer is complementary to and capable of hybridizing to a selected target nucleic acid, and
 - at least one of said first or said second oligomers has a non-linear secondary structure or is part of a multiple oligomer assembly.
2. The composition of claim 1 wherein said first and said second oligomers are a complementary pair of siRNA oligomers.
3. The composition of claim 1 wherein said first and said second oligomers are an antisense/sense pair of oligomers.
4. The composition of claim 1 wherein each of said first and second oligomers has 12 to 50 nucleotides.
5. The composition of claim 1 wherein each of said first and second oligomers has 15 to 30 nucleotides.
6. The composition of claim 1 wherein each of said first and second oligomers has 21 to 24 nucleotides.
7. The composition of claim 1 wherein said first oligomer is an antisense oligomer.
8. The composition of claim 7 wherein said second oligomer is a sense oligomer.
9. The composition of claim 7 wherein said second oligomer has a plurality of ribose nucleotide units.

10. The composition of claim 1 wherein said first oligomer has a non-linear secondary structure or is part of a multiple oligomer assembly.

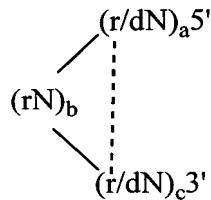
11. The composition of claim 1 wherein the oligomer having a nonlinear secondary structure is a circular oligomer comprising parallel and antiparallel binding domains.

12. The composition of claim 1 wherein the oligomer having a nonlinear secondary structure is a circular oligomer that cannot convert to a linear oligomer.

13. The composition of claim 1 wherein the oligomer having a nonlinear secondary structure is a circular oligomer that comprises an internal ribosome entry site.

14. The composition of claim 1 wherein the oligomer having a nonlinear secondary structure is a circular oligomer that comprises at least one photocleavable group wherein the oligomer is intramolecularly bonded by the photocleavable group.

15. The composition of claim 1 wherein the oligomer having a nonlinear secondary structure is an oligomer of the following structure:



wherein

$(r/dN)_a$ and $(r/dN)_c$ represent series of ribonucleotides or deoxyribonucleotides and $(rN)_b$ represents a series of ribonucleotides;

a, b, and c are numbers of nucleotides in the series, and b is ≥ 1 , a is ≥ 35 , and c is ≥ 10 ;

the series of ribonucleotides or deoxyribonucleotides $(r/dN)_a$ includes a series of ribonucleotides or deoxyribonucleotides that is substantially complementary to the series of ribonucleotides or deoxyribonucleotides $(r/dN)_c$ and the dashed line represents non-covalent bonding between the complementary ribonucleotide or deoxyribonucleotide series; and

the solid lines represent covalent phosphodiester bonds.

16. The composition of claim 1 wherein the oligomer having a nonlinear secondary structure is an oligomer comprising a promoter and encoding a stem loop.

17. The composition of claim 1 wherein the oligomer having a nonlinear secondary structure is an oligomer comprising a stem loop structure in which the loop domain comprises at least one parallel binding domain separated by at least three nucleotides from an antiparallel binding domain.

18. The composition of claim 1 wherein the oligomer having a nonlinear secondary structure is an oligomer that hybridizes with an RNA sequence to form a pseudo half-knot.

19. The composition of claim 1 wherein the oligomer having a nonlinear secondary structure is an oligomer comprising a long RNA segment and a short RNA segment that forms a hairpin having the long RNA segment at the 5' end and the short RNA segment at the 3' end.

20. The composition of claim 1 wherein the oligomer having a nonlinear secondary structure is an oligomer comprising a long RNA segment and a short RNA segment that forms a hairpin having the short RNA segment at the 5' end and the long RNA segment at the 3' end.

21. The composition of claim 1 wherein the oligomer that is part of a multiple oligomer assembly is part of a nucleic acid multimer comprising:

at least one first single-stranded oligomer that is capable of hybridizing specifically to a first single-stranded nucleic acid sequence of interest; and

a multiplicity of second single-stranded oligomers each of which is capable of hybridizing specifically to a second single-stranded nucleic acid sequence of interest, wherein the first single-stranded oligomer is bonded directly or indirectly to the multiplicity of second single-stranded oligomers only via covalent bonds.

22. The composition of claim 1 wherein the oligomer that is part of a multiple oligomer assembly is part of polynucleic acid structure with symmetrical intermolecular contacts formed from joining antiparallel double crossover molecules.

23. The composition of claim 1 wherein the oligomer that is part of a multiple oligomer assembly is part of a branched or multiply connected macromolecular structure comprising a plurality of oligomers wherein at least one oligomer comprises a target binding sequence and at least two oligomers comprise signal generation moieties that directly or indirectly generate a detectable signal in the presence of a target molecule.

24. The composition of claim 1 wherein the oligomer that is part of a multiple oligomer assembly is part of a polynucleotide matrix comprising a plurality of polynucleotide monomers bonded together by hybridization; each polynucleotide monomer having an intermediate region comprising a linear, double stranded waist region having a first end and a second end, said first end terminating with two single stranded hybridization regions, each from one strand of the waist region, and said second end terminating with one or two single stranded hybridization regions, each from one strand of the waist region; and each polynucleotide monomer is hybridization bonded to at least one other polynucleotide monomer at at least one such hybridization region.

25. The composition of claim 1 wherein the oligomer that is part of a multiple oligomer assembly is part of a nucleic acid multimer comprising one or more nucleic acid molecules that together comprise at least two separate target specific regions that hybridize to a target nucleic acid sequence and at least two distinct arm regions that do not hybridize with the target nucleic acid but possess complementary regions that hybridize with one another.

26. The composition of claim 1 wherein the oligomer that is part of a multiple oligomer assembly is part of a polynucleotide matrix having a plurality of single-stranded hybridization arms, said matrix being comprised of a plurality of matrix polynucleotide monomers bonded together by hybridization bonding to form an initial matrix which is then optionally cross-linked so that the matrix is bonded via intermolecular base pairing or intermolecular base pairing and covalent cross-links; each monomer, prior to being so bonded to other monomers, having at least three single-stranded hybridization regions; in said initial matrix each monomer is hybridization

bonded to at least one other monomer and when hybridization bonded to more than one such region of the same monomer, there is an intermediate region where the two monomers are not bonded; wherein each monomer, prior to hybridization bonding to other monomer(s), has a linear double stranded waist region having a first end and a second end, said waist region bonded by hybridization bonding, either fully along its length or including single-stranded portions intermediate to the ends, said first end terminating with two single-stranded hybridization regions and said second end terminating with one or two single-stranded hybridization region(s), each from a strand of the waist region.

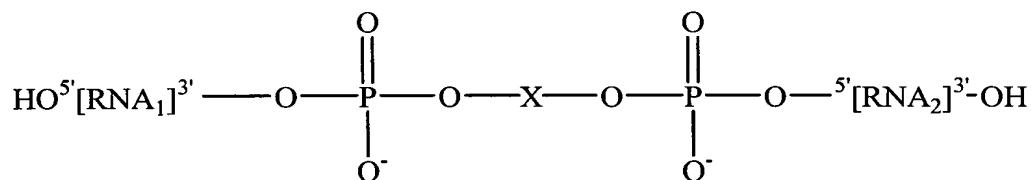
27. The composition of claim 1 wherein the oligomer that is part of a multiple oligomer assembly is part of a polynucleotide binding composition comprising:

two to five oligomers with an overall length of 12 to 120 nucleotides, each component comprising:

an oligomer moiety comprising at least 6 nucleotides, and

at least one terminal binding moiety linked by a short flexible linker having no more than from 2 to 8 carbon atoms to a 5' or 3' terminus of said oligomer moiety, each terminal binding moiety being a member of a pair of terminal binding moieties that spontaneously forms a stable non-covalent complex with one another when said components of said composition specifically bind to a target polynucleotide in a contiguous end-to-end fashion such that each pair of terminal binding moieties is brought into juxtaposition.

28. The composition of claim 1 wherein the oligomer that is part of a multiple oligomer assembly is part of a polynucleotide assembly of the following structure:



wherein

RNA₁ is a first strand of RNA,

RNA₂ is a second strand of RNA, and

X comprises a selectable cleavage site which: (a) is chemically cleavable; (b) is other than a phosphodiester linkage; and (c) provides for a complete break between adjacent nucleotides in the reagent upon cleavage.

29. The composition of claim 1 wherein the oligomer that is part of a multiple oligomer assembly is part of a multiple oligomer assembly comprising:

at least one oligomer moiety capable of specifically hybridizing to a target polynucleotide with a Watson-Crick binding component and a Hoogsteen- or a reverse Hoogsteen-binding component; or at least two oligomer moieties designated as OL1 and OL2 linked to a hinge region designated as G wherein at least one oligomer moiety has a Watson-Crick binding component and at least one oligomer moiety has a Hoogsteen- or a reverse Hoogsteen-binding component; and

at least one pair of non-oligomer binding moieties, each pair of said binding moieties comprising a first binding moiety and a second binding moiety, the first binding moiety being covalently linked to an oligomer moiety and the second binding moiety being covalently linked to an oligomer moiety, wherein a stable covalent or non-covalent linkage is formed between the first binding moiety and the second binding moiety of the pair when the first and second binding moieties of the pair are brought into juxtaposition by the specific hybridization to the target polynucleotide of at least one or at least two oligomer moieties, wherein said multiple oligomer assembly has the formula:

X-OL1-G-OL2-Y

wherein:

OL1 and OL2 are oligomers specific for said target polynucleotide; G is a hinge region which links OL1 to OL2 so as to permit specific hybridization of OL1 and OL2 to their respective target polynucleotides; and

X and Y are non-oligomer binding moieties such that X and Y form a stable covalent or non-covalent linkage or complex whenever they are brought into juxtaposition by the hybridization of OL1 and OL2 to said target polynucleotide.

30. The composition of claim 1 wherein the oligomer that is part of a multiple oligomer assembly is part of a multiple oligomer assembly comprising an optional spacer for attaching a double-stranded oligomer to a solid support, and oligomer attached to the spacer and further attached to a second complementary oligomer by means of a flexible linker such that the two oligomer portions exist in a double-stranded configuration.

31. The composition of claim 1 wherein the oligomer that is part of a multiple oligomer assembly is part of polynucleotide assembly comprising a double-stranded oligomer having either one protruding nucleotide sequence that is a recognition site for a restriction endonuclease at one end of the duplex or two protruding nucleotide sequences that are recognition sites for the same or different restriction endonucleases at opposite ends of the duplex.

32. The composition of claim 1 wherein the oligomer that is part of a multiple oligomer assembly is part of a multiple oligomer assembly comprising a first nucleotide sequence complementary to a first portion of a target nucleotide sequence, a second nucleotide sequence complementary to a portion of the target nucleotide sequence other than and non-contiguous with the first portion, and means for covalently attaching the first and second sequences when the sequences are hybridized with the target nucleotide sequences.

33. The composition of claim 1 wherein the oligomer that is part of a multiple oligomer assembly is part of a multiple oligomer assembly comprising first and second oligomers joined by a bridging nucleic acid sequence wherein the bridging nucleic acid sequence is complementary to and hybridizes to sequences in the termini of each of the first and second oligomers.

34. The composition of claim 1 wherein the oligomer that is part of a multiple oligomer assembly is part of a multiple oligomer assembly comprising a first nucleotide located either on a first strand of complementary oligomer strands or on a single oligomer strand, a second nucleotide located on a further strand of the complementary strands or on the single strand at a site distal to the first nucleotide, a first bond means located on a sugar moiety of the first nucleotide and a second bond means located on a sugar moiety of the second nucleotide, wherein a covalent cross-linkage connects the first and second bond means.

35. The composition of claim 1 wherein the oligomer that is part of a multiple oligomer assembly is part of a multiple oligomer assembly comprising:

a first streptavidin or avidin molecule having a plurality of first biotinylated single-stranded nucleic acids bound to the first streptavidin or avidin molecule;

a plurality of second biotinylated single-stranded nucleic acids bound to a second streptavidin or avidin molecule, at least one of said second nucleic acids hybridizing with a complementary sequence of one of said first nucleic acids; and

a functional group attached to a third single-stranded nucleic acid, said third single-stranded nucleic acid hybridizing with a complementary sequence of one of said second single-stranded nucleic acids.

36. A pharmaceutical composition comprising the composition of claim 1 and a pharmaceutically acceptable carrier.

37. A method of modulating the expression of a target nucleic acid in a cell comprising contacting said cell with a composition of claim 1.

38. A method of treating or preventing a disease or disorder associated with a target nucleic acid comprising administering to an animal having or predisposed to said disease or disorder a therapeutically effective amount of a composition of claim 1.

39. A composition comprising an oligomer complementary to and capable of hybridizing to a selected target nucleic acid and at least one protein, said protein comprising at least a portion of a RNA-induced silencing complex (RISC), wherein:

said oligomer has a non-linear secondary structure or is part of a multiple oligomer assembly.

40. The composition of claim 39 wherein said oligomer is an antisense oligomer.

41. The composition of claim 39 wherein said oligomer has 12 to 50 nucleotides.

42. The composition of claim 39 wherein said oligomer has 15 to 30 nucleotides.

43. The composition of claim 39 wherein said oligomer has 21 to 24 nucleotides.

44. The composition of claim 39 including a further oligomer, wherein said further oligomer is complementary to and hydrizable to said oligomer.

45. The composition of claim 44 wherein said further oligomer is a sense oligomer.

46. The composition of claim 44 wherein said further oligomer is an oligomer having a plurality of ribose nucleotide units.

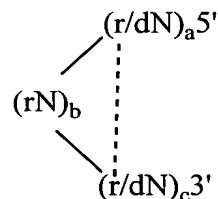
47. The composition of claim 39 wherein the oligomer is a circular oligomer comprising parallel and antiparallel binding domains.

48. The composition of claim 39 wherein the oligomer is a circular oligomer that cannot convert to a linear oligomer.

49. The composition of claim 39 wherein the oligomer is a circular oligomer that comprises an internal ribosome entry site.

50. The composition of claim 39 wherein the oligomer is a circular oligomer that comprises at least one photocleavable group wherein the oligomer is intramolecularly bonded by the photocleavable group.

51. The composition of claim 39 wherein the oligomer is an oligomer of the following structure:



wherein

(r/dN)_a and (r/dN)_c represent series of ribonucleotides or deoxyribonucleotides and (rN)_b represents a series of ribonucleotides;

a, b, and c are numbers of nucleotides in the series, and b is ≥ 1 , a is ≥ 35 , and c is ≥ 10 ;

the series of ribonucleotides or deoxyribonucleotides (r/dN)_a includes a series of ribonucleotides or deoxyribonucleotides that is substantially complementary to the series of ribonucleotides or deoxyribonucleotides (r/dN)_c and the dashed line represents non-covalent bonding between the complementary ribonucleotide or deoxyribonucleotide series; and

the solid lines represent covalent phosphodiester bonds.

52. The composition of claim 39 wherein the oligomer comprises a promoter and encodes a stem loop.

53. The composition of claim 39 wherein the oligomer comprises a stem loop structure in which the loop domain comprises at least one parallel binding domain separated by at least three nucleotides from an antiparallel binding domain.

54. The composition of claim 39 wherein the oligomer hybridizes with an RNA sequence to form a pseudo half-knot.

55. The composition of claim 39 wherein the oligomer is an oligomer comprising a long RNA segment and a short RNA segment that forms a hairpin having the long RNA segment at the 5' end and the short RNA segment at the 3' end.

56. The composition of claim 39 wherein the oligomer is an oligomer comprising a long RNA segment and a short RNA segment that forms a hairpin having the short RNA segment at the 5' end and the long RNA segment at the 3' end.

57. The composition of claim 39 wherein the oligomer is part of a nucleic acid multimer comprising:

at least one first single-stranded oligomer that is capable of hybridizing specifically to a first single-stranded nucleic acid sequence of interest; and

a multiplicity of second single-stranded oligomers each of which is capable of hybridizing specifically to a second single-stranded nucleic acid sequence of interest, wherein the first single-stranded oligomer is bonded directly or indirectly to the multiplicity of second single-stranded oligomers only via covalent bonds.

58. The composition of claim 39 wherein the oligomer is part of polynucleic acid structure with symmetrical intermolecular contacts formed from joining antiparallel double crossover molecules.

59. The composition of claim 39 wherein the oligomer is part of a branched or multiply connected macromolecular structure comprising a plurality of oligomers wherein at least one oligomer comprises a target binding sequence and at least two oligomers comprise signal generation moieties that directly or indirectly generate a detectable signal in the presence of a target molecule.

60. The composition of claim 39 wherein the oligomer is part of a polynucleotide matrix comprising a plurality of polynucleotide monomers bonded together by hybridization; each polynucleotide monomer having an intermediate region comprising a linear, double stranded waist region having a first end and a second end, said first end terminating with two single stranded hybridization regions, each from one strand of the waist region, and said second end terminating with one or two single stranded hybridization regions, each from one strand of the waist region; and each polynucleotide monomer is hybridization bonded to at least one other polynucleotide monomer at at least one such hybridization region.

61. The composition of claim 39 wherein the oligomer is part of a nucleic acid multimer comprising one or more nucleic acid molecules that together comprise at least two separate target specific regions that hybridize to a target nucleic acid sequence and at least two distinct arm regions that do not hybridize with the target nucleic acid but possess complementary regions that hybridize with one another.

62. The composition of claim 39 wherein the oligomer is part of a polynucleotide matrix having a plurality of single-stranded hybridization arms, said matrix being comprised of a

plurality of matrix polynucleotide monomers bonded together by hybridization bonding to form an initial matrix which is then optionally cross-linked so that the matrix is bonded via intermolecular base pairing or intermolecular base pairing and covalent cross-links; each monomer, prior to being so bonded to other monomers, having at least three single-stranded hybridization regions; in said initial matrix each monomer is hybridization bonded to at least one other monomer and when hybridization bonded to more than one such region of the same monomer, there is an intermediate region where the two monomers are not bonded; wherein each monomer, prior to hybridization bonding to other monomer(s), has a linear double stranded waist region having a first end and a second end, said waist region bonded by hybridization bonding, either fully along its length or including single-stranded portions intermediate to the ends, said first end terminating with two single-stranded hybridization regions and said second end terminating with one or two single-stranded hybridization region(s), each from a strand of the waist region.

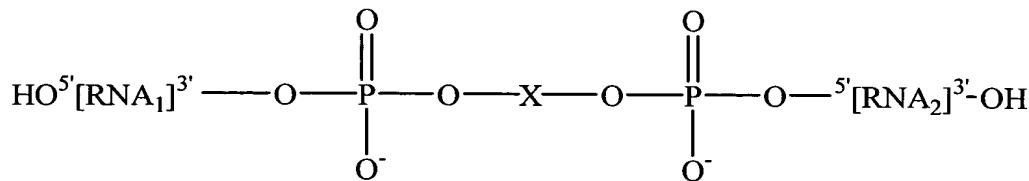
63. The composition of claim 39 wherein the oligomer is part of a polynucleotide binding composition comprising:

two to five oligomers with an overall length of 12 to 120 nucleotides, each component comprising:

an oligomer moiety comprising at least 6 nucleotides, and

at least one terminal binding moiety linked by a short flexible linker having no more than from 2 to 8 carbon atoms to a 5' or 3' terminus of said oligomer moiety, each terminal binding moiety being a member of a pair of terminal binding moieties that spontaneously forms a stable non-covalent complex with one another when said components of said composition specifically bind to a target polynucleotide in a contiguous end-to-end fashion such that each pair of terminal binding moieties is brought into juxtaposition.

64. The composition of claim 39 wherein the oligomer is part of a polynucleotide assembly of the following structure:



wherein

RNA_1 is a first strand of RNA,

RNA_2 is a second strand of RNA, and

X comprises a selectable cleavage site which: (a) is chemically cleavable; (b) is other than a phosphodiester linkage; and (c) provides for a complete break between adjacent nucleotides in the reagent upon cleavage.

65. The composition of claim 39 wherein the oligomer is part of a multiple oligomer assembly comprising:

at least one oligomer moiety capable of specifically hybridizing to a target polynucleotide with a Watson-Crick binding component and a Hoogsteen- or a reverse Hoogsteen-binding component; or at least two oligomer moieties designated as OL1 and OL2 linked to a hinge region designated as G wherein at least one oligomer moiety has a Watson-Crick binding component and at least one oligomer moiety has a Hoogsteen- or a reverse Hoogsteen-binding component; and

at least one pair of non-oligomer binding moieties, each pair of said binding moieties comprising a first binding moiety and a second binding moiety, the first binding moiety being covalently linked to an oligomer moiety and the second binding moiety being covalently linked to an oligomer moiety, wherein a stable covalent or non-covalent linkage is formed between the first binding moiety and the second binding moiety of the pair when the first and second binding moieties of the pair are brought into juxtaposition by the specific hybridization to the target polynucleotide of at least one or at least two oligomer moieties, wherein said multiple oligomer assembly has the formula:

X-OL1-G-OL2-Y

wherein:

OL1 and OL2 are oligomers specific for said target polynucleotide; G is a hinge region

which links OL1 to OL2 so as to permit specific hybridization of OL1 and OL2 to their respective target polynucleotides; and

X and Y are non-oligomer binding moieties such that X and Y form a stable covalent or non-covalent linkage or complex whenever they are brought into juxtaposition by the hybridization of OL1 and OL2 to said target polynucleotide.

66. The composition of claim 39 wherein the oligomer is part of a multiple oligomer assembly comprising an optional spacer for attaching a double-stranded oligomer to a solid support, and oligomer attached to the spacer and further attached to a second complementary oligomer by means of a flexible linker such that the two oligomer portions exist in a double-stranded configuration.

67. The composition of claim 39 wherein the oligomer is part of polynucleotide assembly comprising a double-stranded oligomer having either one protruding nucleotide sequence that is a recognition site for a restriction endonuclease at one end of the duplex or two protruding nucleotide sequences that are recognition sites for the same or different restriction endonucleases at opposite ends of the duplex.

68. The composition of claim 39 wherein the oligomer is part of a multiple oligomer assembly comprising a first nucleotide sequence complementary to a first portion of a target nucleotide sequence, a second nucleotide sequence complementary to a portion of the target nucleotide sequence other than and non-contiguous with the first portion, and means for covalently attaching the first and second sequences when the sequences are hybridized with the target nucleotide sequences.

69. The composition of claim 39 wherein the oligomer is part of a multiple oligomer assembly comprising first and second oligomers joined by a bridging nucleic acid sequence wherein the bridging nucleic acid sequence is complementary to and hybridizes to sequences in the termini of each of the first and second oligomers.

70. The composition of claim 39 wherein the oligomer is part of a multiple oligomer assembly comprising a first nucleotide located either on a first strand of complementary

oligomer strands or on a single oligomer strand, a second nucleotide located on a further strand of the complementary strands or on the single strand at a site distal to the first nucleotide, a first bond means located on a sugar moiety of the first nucleotide and a second bond means located on a sugar moiety of the second nucleotide, wherein a covalent cross-linkage connects the first and second bond means.

71. The composition of claim 39 wherein the oligomer is part of a multiple oligomer assembly comprising:

a first streptavidin or avidin molecule having a plurality of first biotinylated single-stranded nucleic acids bound to the first streptavidin or avidin molecule;

a plurality of second biotinylated single-stranded nucleic acids bound to a second streptavidin or avidin molecule, at least one of said second nucleic acids hybridizing with a complementary sequence of one of said first nucleic acids; and

a functional group attached to a third single-stranded nucleic acid, said third single-stranded nucleic acid hybridizing with a complementary sequence of one of said second single-stranded nucleic acids.

72. A pharmaceutical composition comprising the composition of claim 39 and a pharmaceutically acceptable carrier.

73. A method of modulating the expression of a target nucleic acid in a cell comprising contacting said cell with a composition of claim 39.

74. A method of treating or preventing a disease or disorder associated with a target nucleic acid comprising administering to an animal having or predisposed to said disease or disorder a therapeutically effective amount of a composition of claim 39.

75. An oligomer having at least a first region and a second region, wherein
said first region of said oligomer is complementary to and capable of hybridizing with
said second region of said oligomer,

at least a portion of said oligomer is complementary to and capable of hybridizing to a selected target nucleic acid, and

said oligomer has a non-linear secondary structure or is part of a multiple oligomer assembly.

76. The oligomer of claim 75 wherein each of said first and said second regions is at least 10 nucleotides.

77. The oligomer of claim 75 wherein said first region in a 5' to 3' direction is complementary to said second region in a 3' to 5' direction.

78. The oligomer of claim 75 wherein said oligomer includes a hairpin structure.

79. The oligomer of claim 75 wherein said first region of said oligomer is spaced from said second region of said oligomer by a third region and where said third region comprises at least two nucleotides.

80. The oligomer of claim 75 wherein said first region of said oligomer is spaced from said second region of said oligomer by a third region and where said third region comprises a non-nucleotide region.

81. A pharmaceutical composition comprising the oligomer of claim 75 and a pharmaceutically acceptable carrier.

82. A method of modulating the expression of a target nucleic acid in a cell comprising contacting said cell with the oligomer of claim 75.

83. A method of treating or preventing a disease or disorder associated with a target nucleic acid comprising administering to an animal having or predisposed to said disease or disorder a therapeutically effective amount of the oligomer of claim 75.